Original article

Kosin Medical Journal 2024;39(2):99-111
pISSN: 2005-9531 • eISSN: 2586-7024
https://doi.org/10.7180/kmj.24.106

KMJ
KOSIN MEDICAL JOURNAL

Clinical features of coronavirus disease 2019 in Korean pediatric patients: a single-center retrospective study

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Background: To address the public's fear of coronavirus disease 2019 (COVID-19), understanding the clinical features of the disease is essential. However, research on the clinical features of COVID-19, including illness duration and post-acute COVID-19, in Korean pediatric patients has been limited. Therefore, this study investigated the clinical features of COVID-19 based on the medical records of pediatric patients with a history of COVID-19 who visited a single center.

Methods: In total, 311 patients were included in this study. The presence and duration of 19 symptoms were examined. Additionally, clinical features were investigated by dividing the patients into different age ranges. Patients aged 6 and above were further categorized according to the presence of asthma, while adolescent patients were divided into vaccinated and unvaccinated groups.

Results: Fever and cough were the most common symptoms. The mean illness duration was 2–4 days. Only 3.5% of the patients were asymptomatic. Post-acute COVID-19 was observed in 13.2% of the patients. The incidence of most symptoms tended to increase with age. Post-acute COVID-19 was observed more frequently in patients with asthma than in those without asthma. Vaccinated patients experienced less fever, vomiting, and fatigue than unvaccinated patients.

Conclusions: Our data suggest that most patients had mild disease lasting less than a week, and the clinical course may differ depending on the presence of asthma. The findings also indicate that vaccination may alleviate the symptoms of COVID-19 in breakthrough infections.

Keywords: Adolescent; Child; COVID-19; Korea; Signs and symptoms

Introduction

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The World Health Organization declared COVID-19 pandemic on March 11, 2020 [1]. In Korea, the number of daily confirmed cases reached a maximum of 621,035 in mid-March 2022 and gradually decreased afterwards; however, it saw a resurgence beginning in the summer of 2023, coinciding with the relaxation of the mask mandate. According to the Korea Disease Control and Prevention Agency (KDCA), as of August 31, 2023, the cumulative number of confirmed cases stood at 34,571,873. Among them, 3,270,242 involved children aged 0–9 years, and 4,246,913 involved children aged 10–19 years, accounting for 19% of the total cumulative cases [2].

Pediatric patients with COVID-19 experience a milder course of the disease than that in adults [3,4]. However, anxiety surrounding COVID-19 has become widespread due to disruptions in daily routines. A study on anxiety among

Received: January 12, 2024; **Revised:** May 16, 2024; **Accepted:** May 17, 2024
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Korean adolescents during the COVID-19 pandemic found that the fear of infection was one of the factors related to anxiety [5]. One of the contributing factors to this fear of COVID-19 is ignorance about the disease. To overcome this fear, the public and physicians must possess sufficient knowledge about COVID-19 [6].

Hence, this study aimed to provide a trigger point for research on the general course of COVID-19 in children and adolescents in Korea by investigating the clinical features of patients with a history of COVID-19 who visited a single healthcare center.

Methods

Ethical statements: This study was approved by the Institutional Review Board (IRB) of the Daegu Catholic University Medical Center (IRB No: CR-22-135). The requirement for patient consent was waived because this study was a retrospective chart review study in which there are minimal risks to subjects.

1. Patients and study design

Among patients who visited the outpatient clinic of the Department of Pediatrics at Daegu Catholic University Medical Center from March 1 to May 31, 2022, we screened 317 patients under the age of 20 who reported having previously been diagnosed with COVID-19 using SARS-CoV-2 rapid antigen kit for professional use or polymerase chain reaction. We excluded four patients within 7 days of the COVID-19 diagnosis because the follow-up period was too short and could provide inaccurate information about the presence or duration of symptoms. Two patients suspected of having other superimposed infections within 1 week before and after the COVID-19 diagnosis were also excluded. Finally, 311 medical records were analyzed retrospectively. The following demographic data and clinical symptoms were obtained from the electronic medical records: sex, age, history of vaccination against COVID-19, fever, cough, runny or stuffy nose, dyspnea, chest discomfort, chest pain, myalgia, headache, dizziness, sore eyes, sore throat, nausea, vomiting, abdominal pain, diarrhea, loss of smell, loss of taste, fatigue, COVID-19-associated hospitalization, and underlying diseases. Loss of smell and taste included both partial and complete loss. Clinical symptoms that rely on verbal expression capability were evaluated for individuals aged 3 years and older. Underlying diseases were evaluated based on medical records; however, only patients who reported being diagnosed with asthma and whose bronchial hyperresponsiveness was confirmed through a methacholine provocation test were classified into the asthma group. Bronchial hyperresponsiveness was defined as a provocative concentration of methacholine causing a 20% fall in forced expiratory volume in 1 second (PC20) ≤16 mg/mL [7]. Patients with no history of asthma in their medical records were classified into the non-asthma group. Post-acute COVID-19 was defined as the persistence of one or more clinical symptoms for over 4 weeks [8].

Patients were divided into infant and toddler (aged 0–2), preschooler (aged 3–5), middle childhood (aged 6–11), and adolescent (aged 12 years and older) groups to compare the symptoms of COVID-19 by age. In addition, children aged 6 years and older were divided into an asthma group and a non-asthma group, while adolescents were divided into a vaccinated group that had completed two primary doses and an unvaccinated group that had not. The clinical features of the two groups were compared.

2. Statistical analysis

The chi-square test was used to compare categorical variables. The Fisher exact test was performed if more than 20% of the cells had an expected frequency of less than five. When comparing continuous data from the two groups, the independent samples *t*-test was performed if the distribution of the variable was normal, and the Mann-Whitney *U* test was used if the distribution was not normal. The one-way analysis of variance was performed to compare normally distributed continuous variables between three or more groups, and the Kruskal-Wallis test was used to compare non-normally distributed continuous data. Post-hoc analysis was performed to compare three or more groups. Variables with fewer than 20 available data points in any group were not analyzed to achieve alpha levels of 0.05 and 80% power when comparing the groups. The Cochran-Armitage trend test was used to analyze trends between age categories.

When comparing the asthma and non-asthma groups, age and sex were adjusted for using 1:1 propensity score matching.

When comparing the vaccinated and unvaccinated groups, propensity score matching could not be performed

because the number of unvaccinated participants was smaller than the number of vaccinated participants. Therefore, to adjust for age and sex in the clinical features that showed differences in the univariate analysis, age, sex, and vaccination history were added as covariates, and multivariate regression analysis was performed.

Statistical analyses were performed using IBM SPSS Statistics version 25.0 software (IBM Co.) and R version 4.2.0 software package (R Project for Statistical Computing). A *p*-value less than 0.05 was considered statistically significant. When post-hoc analysis was performed, the Bonferroni correction was applied to adjust for type I errors. A *p*-value <0.008 in the comparison of the four groups and a *p*-value <0.017 in the comparison of the three groups were considered statistically significant.

Results

1. Characteristics of the study population

Table 1 presents the demographic characteristics of the 311 patients included in this study. The median age was 8 years. Considering age categories, those aged 6–11 was the majority (48.9%), followed by those aged 12 and older, those aged 3–5 years, and those aged 0–2 years. One hundred and sixty-seven participants (52.7%) were male. The median duration from COVID-19 diagnosis to the clinic visit was 30 days (interquartile range [IQR], 20–44 days).

According to reports from patients or caregivers, the most common sources of infection were educational institutions or childcare centers (43.4%) and family or relatives (37.3%). Six infections occurred in public places: two in restaurants, three in hospitals, and one in a swimming pool. Concurrent COVID-19 illness in families or cohabitators occurred in 90% of patients.

South Korea has approved the use of SARS-CoV-2 vaccine for children aged 12 years and older since Oct 2021 [9]. Of 73 patients eligible for vaccination, 42 patients (58%) had been vaccinated. Most of those vaccinated patients had completed two primary vaccinations, and three had received booster doses.

The most frequently reported underlying disease was allergic rhinitis (39.2%), followed by precocious puberty (14.8%). All children with immunodeficiency exhibited selective IgG3 deficiency. Genetic comorbidities were Marfan syndrome in one patient, Prader–Willi syndrome in one patient,

Table 1. Demographic characteristics

Characteristic	Value (n=311)
Age at diagnosis (yr)	8 (5–11)
Age category	
0–2 yr	34 (10.9)
3–5 yr	52 (16.7)
6–11 yr	152 (48.9)
≥12 yr	73 (23.4)
Male sex	164 (52.7)
Duration from diagnosis of COVID-19 to clinic visit (day)	30 (20–44)
Probable source of infection	
Education or childcare system	135 (43.4)
Family or relatives	116 (37.3)
Public spaces	6 (1.9)
Unknown	54 (17.4)
Family or cohabitor's history of concurrent COVID-19	
Yes	280 (90.0)
No	25 (8.0)
Unknown	6 (1.9)
Vaccination (n=73)[a]	
Yes	42 (57.5)
No. of vaccinations among those vaccinated	
1	1 (2.4)
2	38 (90.5)
3	3 (7.1)
No	30 (41.1)
Unknown	1 (1.4)
Underlying disease	
Preterm	43 (13.8)
Bronchial asthma	53 (17.0)
Allergic rhinitis	122 (39.2)
Atopic dermatitis	47 (15.1)
Chronic urticaria	5 (1.6)
Postinfectious bronchiolitis obliterans	27 (8.7)
Immunodeficiency	5 (1.6)
Precocious puberty	46 (14.8)
Other endocrine diseases[b]	43 (13.8)
Primary amenorrhea	1 (0.3)
Diseases of the digestive system[c]	3 (1.0)
Epilepsy	5 (1.6)
Muscular dystrophy	1 (0.3)
Hypertension	1 (0.3)
Orthostatic proteinuria	1 (0.3)
Developmental delay	17 (5.5)
Genetic disease	6 (1.9)

Values are presented as median (interquartile range) or number (%).
COVID-19, coronavirus disease 2019.
[a]Considering South Korea's vaccination approval requirements, only those aged 12 or older were analyzed.
[b]This category included 20 patients with growth hormone deficiency, 17 patients with thyroid diseases, three patients with diabetes mellitus, two patients with congenital adrenal hyperplasia, and one patient with hereditary hypertriglyceridemia.
[c]This category included two patients with fatty liver and one patient with Crohn's disease.

Wolf–Hirschhorn syndrome in one patient, Lamb–Shaffer syndrome in one patient, and 3p deletion syndrome in one patient. Thirty-eight patients had no underlying disease.

2. Clinical manifestations

The most common clinical symptom was fever, observed in 263 patients (84.6%), followed by cough (76.2%) and sore throat (56.7%). Rhinorrhea and nasal stuffiness occurred in 44.7% and 46.3% of the patients, respectively. Symptoms lasted for 2–4 days and improved within 7 days. Eleven patients (3.5%) remained asymptomatic. Forty-one patients (13.2%) developed post-acute COVID-19 (Table 2). Hospitalization occurred in four cases, with stays lasting 7 days in two cases, 6 days in one case, and 4 days in one case. Among the 311 patients, 18 were diagnosed with overlapping clinical syndromes. Overlapping syndrome included croup and bronchitis in five patients each, asthma exacerbation in four patients, acute pharyngitis in one patient, and acute gastroenteritis in one patient.

When evaluating patients with post-acute COVID-19, the most prevalent symptom reported was persistent coughing, observed in 26 out of 41 cases (63%). This was followed by fatigue in eight patients (20%), nasal stuffiness in six patients (15%), and headache and rhinorrhea in four patients (10%). Other symptoms included loss of taste, chest discomfort, nausea, sore throat, dyspnea, loss of smell, diarrhea, abdominal pain, dizziness, and myalgia. In addition, one patient reported only a feeling of sputum production lasting more than 4 weeks without any other symptoms (Fig. 1).

3. Clinical features by age category

The symptoms were compared by dividing the patients into four age groups. Fever was significantly less frequent at 12 years of age and older than at 3–5 years of age (p<0.008) and showed a tendency to decrease as age increased (p=0.013). The incidences of cough, nasal stuffiness, chest discomfort, myalgia, headache, dizziness, sore eyes, sore throat, nausea, loss of smell, and loss of taste increased with age. There was no trend in rhinorrhea according to age category, but the 6- to 11-year-old group showed a significantly lower incidence rate than the other groups (p<0.008). The incidence rates of dyspnea, chest pain, vomiting, abdominal pain, diarrhea, and asymptomatic presentation did not differ between the age categories, and there was no trend. The frequency of post-acute COVID-19 tended to increase with age; however, there was no significant

Table 2. Clinical manifestations of the analyzed patients

Variable	No. of patients with data available	No. (%) or median (IQR)
Fever	311	263 (84.6)
Peak value	258	39.0 (38.5–39.8)
Duration (day)	256	2.0 (2.0–3.0)
Cough	311	237 (76.2)
Duration (day)	195	4.0 (2.0–7.0)
Rhinorrhea	311	139 (44.7)
Duration (day)	127	4.0 (3.0–7.0)
Nasal stuffiness	311	144 (46.3)
Duration (day)	133	3.0 (2.5–6.0)
Dyspnea	310	20 (6.5)
Duration (day)	18	3.0 (2.0–5.5)
Chest discomfort[a)]	277	22 (7.9)
Duration (day)	18	3.0 (2.8–7.0)
Chest pain[a)]	277	16 (5.8)
Duration (day)	15	3.0 (2.0–7.0)
Myalgia[a)]	277	69 (24.9)
Duration (day)	64	3.0 (2.0–3.0)
Headache[a)]	277	101 (36.5)
Duration (day)	92	3.0 (2.0–3.0)
Dizziness[a)]	277	61 (22.0)
Duration (day)	58	3.0 (2.0–3.0)
Sore eyes[a)]	277	12 (4.3)
Duration (day)	12	2.5 (1.3–5.0)
Sore throat[a)]	277	157 (56.7)
Duration (day)	150	3.0 (3.0–5.0)
Nausea[a)]	277	32 (11.6)
Duration (day)	30	2.0 (2.0–3.0)
Vomiting	311	31 (10.0)
Duration (day)	30	1.5 (1.0–2.3)
Abdominal paina)	277	29 (10.5)
Duration (day)	27	2.0 (2.0–3.0)
Diarrhea	311	44 (14.1)
Duration (day)	43	2.0 (2.0–4.0)
Loss of smell[a)]	276	17 (6.1)
Duration (day)	15	4.0 (2.0–8.0)
Loss of taste[a)]	277	33 (11.9)
Duration (day)	27	4.0 (2.0–7.0)
Fatigue[a)]	277	88 (31.8)
Duration (day)	77	4.0 (3.0–7.0)
Asymptomatic	311	11 (3.5)
Post-acute COVID-19	311	41 (13.2)
Hospitalization	311	4 (1.3)
Overlapping clinical syndromes	311	18 (5.8)

IQR, interquartile range; COVID-19, coronavirus disease 2019.
[a)]Only 3 years or older.

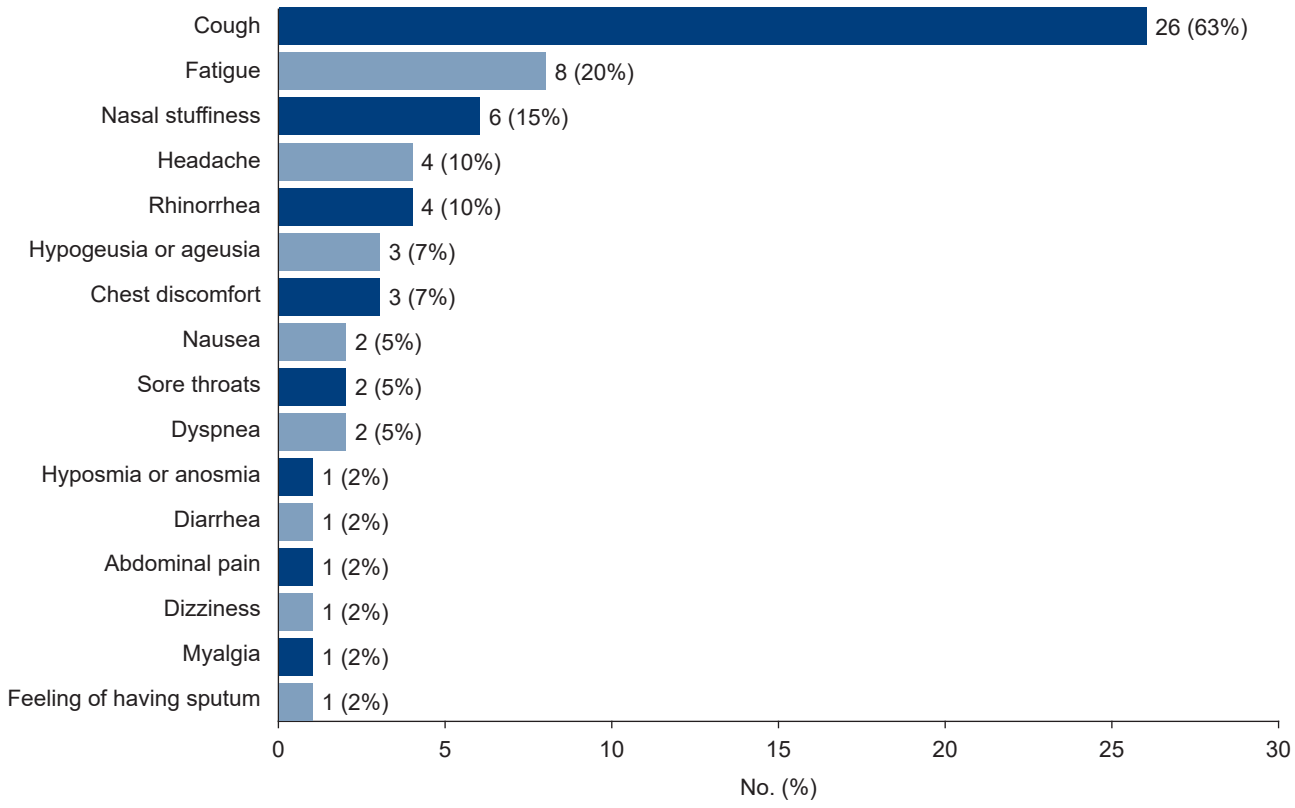

Fig. 1. Proportion of patients with post-acute coronavirus disease 2019 symptoms. If a patient had multiple symptoms, multiple variables corresponding to the symptoms were selected.

difference between the groups (Fig. 2).

4. Clinical features of asthma

There were no significant differences between the two groups regarding the duration from the diagnosis of COVID-19 to the clinic visit, age at diagnosis, sex, or vaccination history (p=0.128, p=0.698, p=1.000, respectively). Allergic rhinitis and atopic dermatitis were more frequently observed in the asthma group than that in the non-asthma group. When comparing clinical features, no significant differences were observed between the two groups for all symptoms, including cough, rhinorrhea, nasal stuffiness, and dyspnea. However, the post-acute COVID-19 rate was significantly higher in the asthma group (22.6%) than in the non-asthma group (3.8%) (p=0.004) (Table 3).

Among the 12 patients with asthma and post-acute COVID-19, six reported only a cough lasting more than 4 weeks, and two reported rhinorrhea and cough lasting more than 4 weeks. The remaining four patients each reported that cough and fatigue, rhinorrhea and chest discomfort, loss of taste, and the feeling of having sputum persisted for more than 4 weeks.

5. Clinical features of vaccination

There was no difference in mean duration from diagnosis of COVID-19 to clinic visit between the vaccinated and unvaccinated groups (p=0.110). The median age of the vaccinated group was 15 years (IQR, 14.0–16.3 years), significantly older than that of the unvaccinated group (13 years old: IQR, 12.0–14.0 years; p=0.001); there was no difference in sex between the groups (Table 4). In the vaccinated group, fever occurred in 24 patients (63.2%) with a peak value of 38.5 °C (IQR, 38.0–39.0 °C), significantly lower than that observed in the 27 unvaccinated patients (87.1%), with a peak value of 39 °C (IQR, 38.1–39.5 °C) (p=0.024, p=0.047, respectively). The frequencies of cough, rhinorrhea, nasal stuffiness, dyspnea, chest discomfort, chest pain, myalgia, headache, dizziness, sore eyes, and sore throat did not differ between

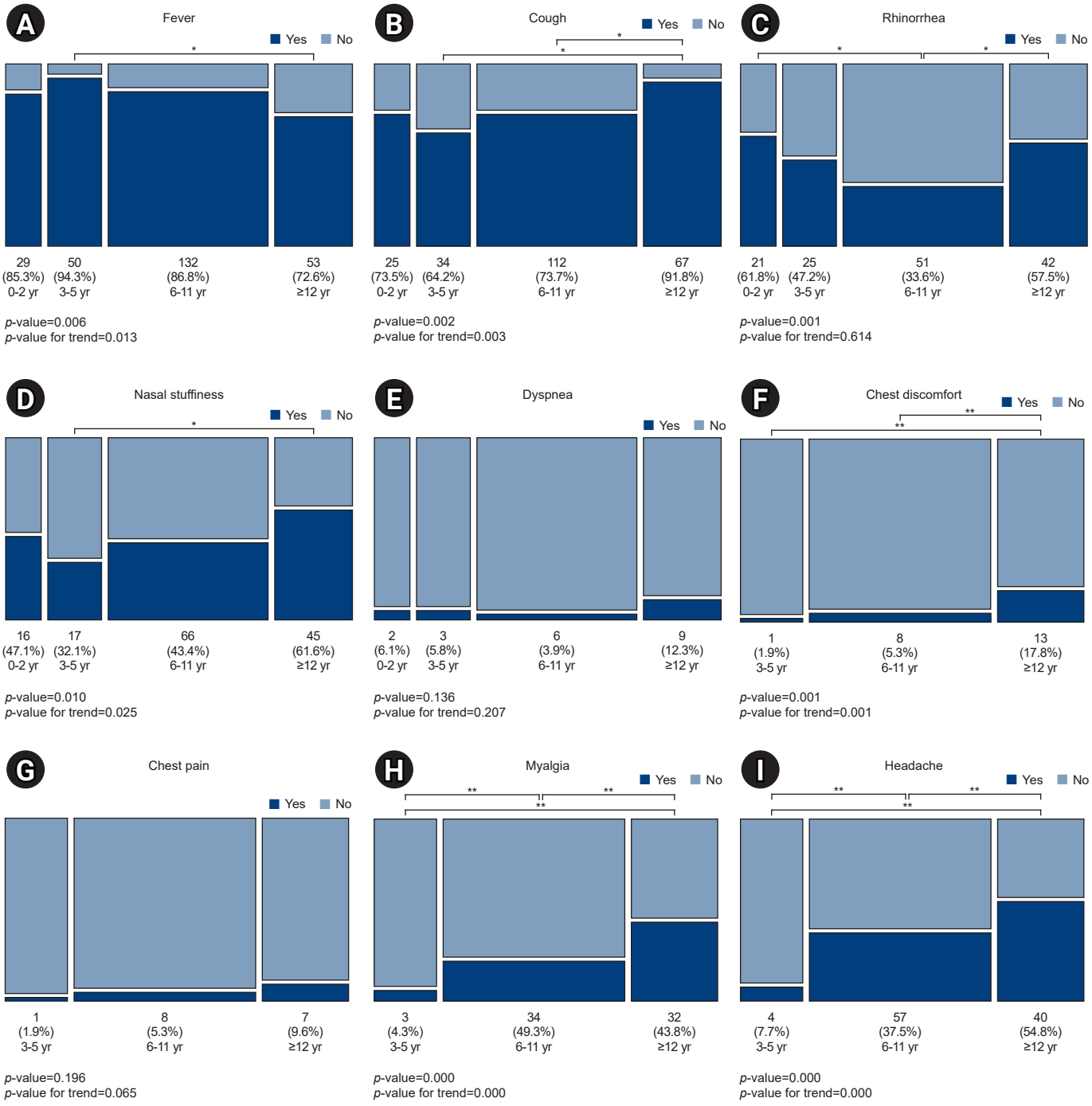

Fig. 2. Clinical features by age category: (A) fever, (B) cough, (C) rhinorrhea, (D) nasal stuffiness, (E) dyspnea, (F) chest discomfort, (G) chest pain, (H) myalgia, (I) headache, (J) dizziness, (K) sore eyes, (L) sore throat, (M) nausea, (N) vomiting, (O) abdominal pain, (P) diarrhea, (Q) loss of smell, (R) loss of taste, (S) fatigue, (T) asymptomatic, and (U) post-acute coronavirus disease 2019 (COVID-19). *p<0.008; **p<0.017. (Continued)

the two groups. Among the gastrointestinal symptoms, the frequency of nausea, abdominal pain, and diarrhea did not differ between the two groups; however, the frequency of vomiting differed significantly between the two groups: one patient (2.6%) in the vaccinated group and seven patients (22.6%) in the unvaccinated group (p=0.019). The frequen-

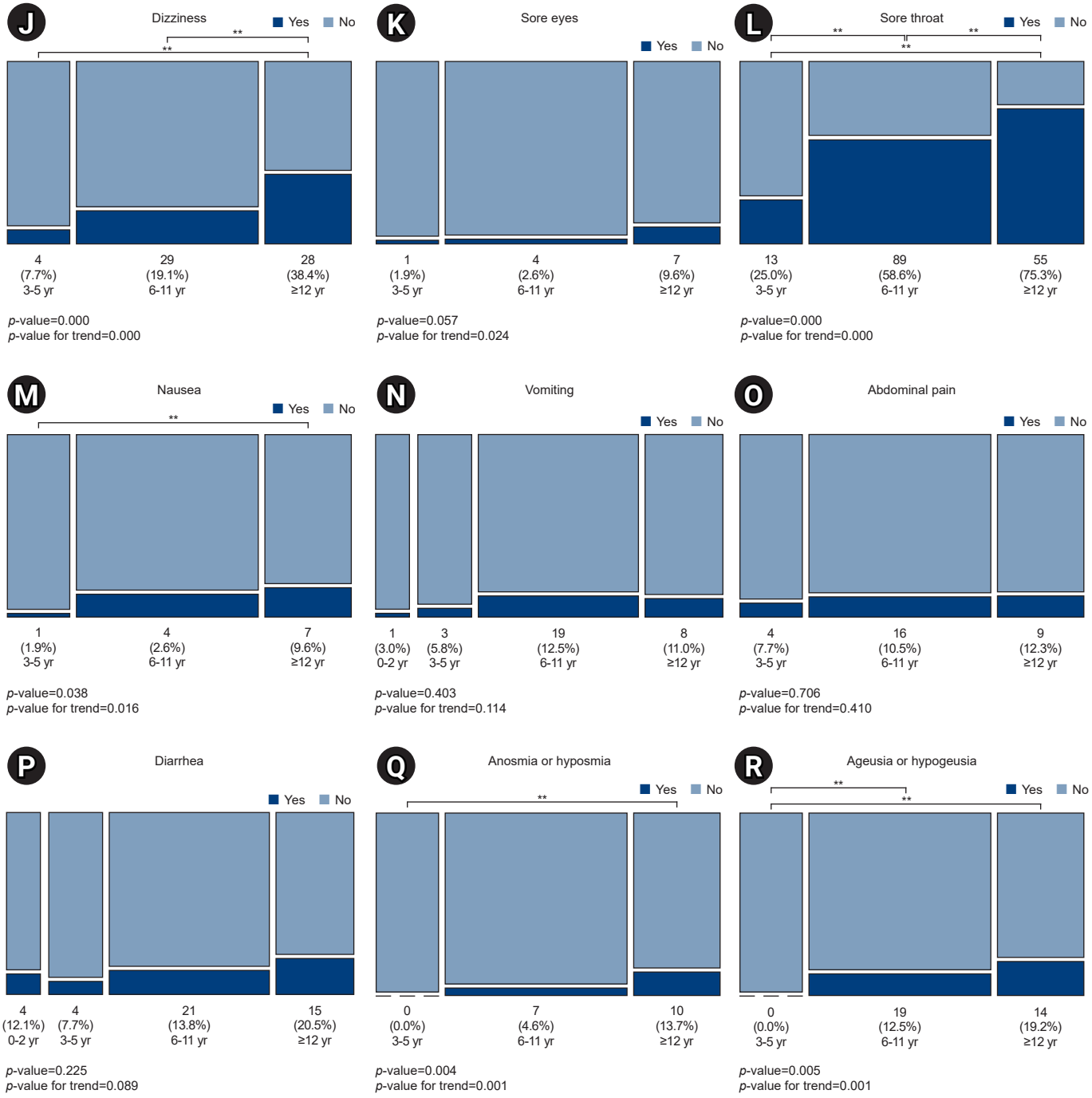

Fig. 2. (Continued from the previous page)

cies of alterations in smell and taste did not differ between the two groups. The frequency of fatigue was significantly lower in the vaccinated group: 15 patients (39.5%) in the vaccinated group and 20 patients (64.5%) in the non-vaccinated group (p=0.038). The incidence rates of asymptomatic and post-acute COVID-19 did not differ between the two groups.

Age and sex adjustments were made to investigate the effects of vaccination on fever, vomiting, and fatigue. In the vaccination group, the independent decrease in the risk of

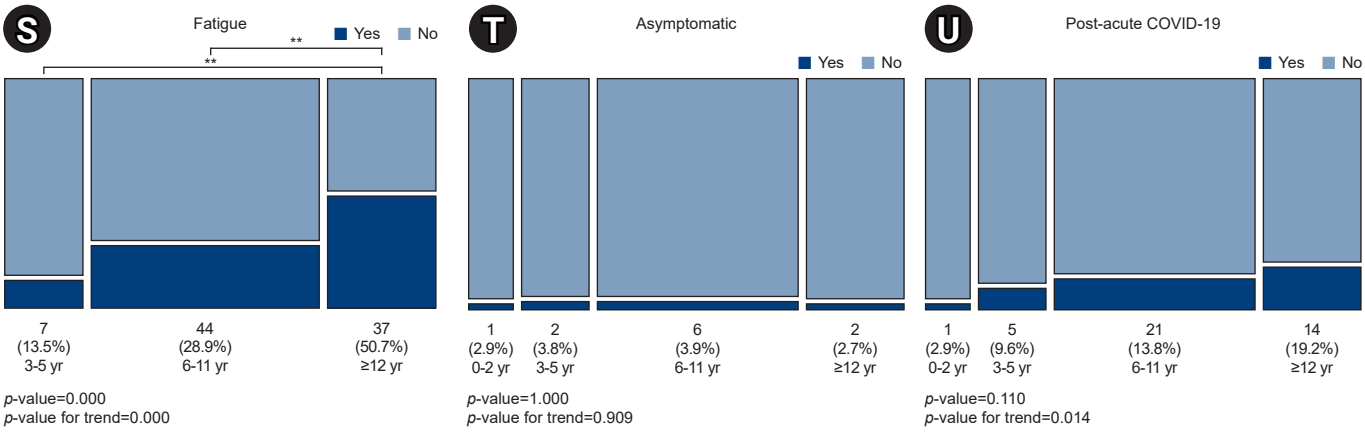

Fig. 2. (Continued from the previous page)

Table 3. Clinical features according to the presence of asthma

Variable	Asthma (n=53)		Non-asthma (n=53)		*p*-value
	No. of patients with data available	No. (%) or median (IQR)	No. of patients with data available	No. (%) or median (IQR)	
Age at diagnosis (yr)	53	9.0 (7.0–12.5)	53	10.0 (7.0–13.0)	0.698
Male sex	53	38 (71.7)	53	38 (71.7)	1.000
Allergic rhinitis	53	45 (84.9)	53	7 (13.2)	0.000
Atopic dermatitis	53	12 (22.6)	53	4 (7.5)	0.030
Vaccination	51	9 (17.6)	53	12 (22.6)	0.526
Fever	53	42 (79.2)	53	42 (79.2)	1.000
Peak value (°C)	42	39.0 (38.3–40.0)	41	39.0 (38.8–39.6)	0.820
Cough	53	44 (83.0)	53	40 (75.5)	0.338
Rhinorrhea	53	26 (49.1)	53	23 (43.4)	0.559
Nasal stuffiness	53	29 (54.7)	53	24 (45.3)	0.331
Dyspnea	53	4 (7.5)	53	1 (1.9)	0.169
Chest discomfort	53	6 (11.3)	53	4 (7.5)	0.506
Chest pain	53	5 (9.4)	53	3 (5.7)	0.462
Myalgia	53	14 (26.4)	53	19 (35.8)	0.294
Headache	53	25 (47.2)	53	22 (41.5)	0.558
Dizziness	53	14 (26.4)	53	15 (28.3)	0.828
Sore eyes	53	1 (1.9)	53	1 (1.9)	1.000
Sore throat	53	33 (62.3)	53	32 (60.4)	0.842
Nausea	53	9 (17.0)	53	3 (5.7)	0.066
Vomiting	53	8 (15.1)	53	5 (9.4)	0.374
Abdominal pain	53	6 (11.3)	53	4 (7.5)	0.506
Diarrhea	53	6 (11.3)	53	6 (11.3)	1.000
Loss of smell	53	1 (1.9)	53	5 (9.4)	0.093
Loss of taste	53	8 (15.1)	53	8 (15.1)	1.000
Fatigue	53	18 (34.0)	53	17 (32.1)	0.836
Asymptomatic	53	2 (3.8)	53	4 (7.5)	0.401
Post-acute COVID-19	53	12 (22.6)	53	2 (3.8)	0.004

IQR, interquartile range; COVID-19, coronavirus disease 2019.

fever was observed regardless of age and sex (odds ratio [OR], 0.25; 95% confidence interval [CI], 0.07–0.88; p=0.030), and the peak value of fever also decreased (β, –0.30; 95% CI, –0.94 to –0.03; p=0.038). The risk of vomiting also decreased inde-

Table 4. Clinical features according to vaccination status

Variables	Vaccinated (n=38)		Unvaccinated (n=31)		*p*-value
	No. of patients with data available	No. (%) or median (IQR)	No. of patients with data available	No. (%) or median (IQR)	
Age at diagnosis (yr)	38	15 (14–16)	31	13 (12–14)	0.001
Male sex	38	16 (42.1)	31	14 (45.2)	0.799
Fever	38	24 (63.2)	31	27 (87.1)	0.024
Peak value (°C)	21	38.5 (38.0–39.0)	27	39 (38.1–39.5)	0.047
Cough	38	35 (92.1)	31	28 (90.3)	1.000
Rhinorrhea	38	24 (63.2)	31	16 (51.6)	0.334
Nasal stuffiness	38	23 (60.5)	31	19 (61.3)	0.948
Dyspnea	38	5 (13.2)	31	3 (9.7)	0.722
Chest discomfort	38	7 (18.4)	31	4 (12.9)	0.743
Chest pain	38	3 (7.9)	31	4 (12.9)	0.692
Myalgia	38	18 (47.4)	31	14 (45.2)	0.855
Headache	38	20 (52.6)	31	19 (61.3)	0.470
Dizziness	38	14 (36.8)	31	14 (45.2)	0.484
Sore eyes	38	3 (7.9)	31	4 (12.9)	0.692
Sore throat	38	30 (78.9)	31	23 (74.2)	0.642
Nausea	38	4 (10.5)	31	7 (22.6)	0.202
Vomiting	38	1 (2.6)	31	7 (22.6)	0.019
Abdominal pain	38	3 (7.9)	31	5 (16.1)	0.452
Diarrhea	38	7 (18.4)	31	8 (25.8)	0.459
Loss of smell	38	5 (13.2)	31	5 (16.1)	0.745
Loss of taste	38	6 (15.8)	31	7 (22.6)	0.473
Fatigue	38	15 (39.5)	31	20 (64.5)	0.038
Asymptomatic	38	1 (2.6)	31	1 (3.2)	1.000
Post-acute COVID-19	38	7 (18.4)	31	5 (16.1)	0.803

IQR, interquartile range; COVID-19, coronavirus disease 2019.

pendent of age and sex in the vaccination group (OR, 0.09; 95% CI, 0.01–0.80; p=0.031). Fatigue was related to both sex (OR, 3.36; 95% CI, 1.19–9.46; p=0.022) and vaccination status (OR, 0.34; 95% CI, 0.12–0.95; p=0.040); the risk of fatigue was lower in females and in patients in the vaccination group.

Discussion

In this study, the median illness duration for all symptoms investigated was 2–4 days. Post-acute COVID-19 was observed in 41 patients (13.2%), and the most common symptom was cough. There were no significant differences in the acute symptoms between the asthma and non-asthma groups; however, the incidence of post-acute COVID-19 was significantly higher in the asthma group. Fever, vomiting, and fatigue were less observed in vaccinated group than that in unvaccinated group.

In general, the most frequently observed symptoms in children and adolescents with COVID-19 were fever (20.6%–80.2%) and cough (33.7%–54.2%) [4,10-12]. Although the frequencies were moderately different, fever (84.6%) and cough (76.2%) were the most common in our study. However, a prospective cohort study in the United Kingdom revealed headache and fatigue as the predominant symptoms (62.2% and 55.0%, respectively) [13]. The mean illness duration was 6 days in foreign studies and 4 days in this study, indicating that the symptoms disappeared within 1 week [4,10,13].

The common cold is a viral illness on the upper respiratory tract such as the nose, sinuses, and throat. In general, the severity of symptoms of cold peaks within 2–3 days, and then the symptoms decrease and disappear [14]. Although it was not compared with a control group consisting of patients with other respiratory viral infections during the same period in this study, based on previous research about the common cold, the duration of illness of COVID-19 in

children and adolescents shown in our study is similar to that of the common cold.

The proportion of asymptomatic patients varied among the studies. Data from hospitalized Korean children showed that 4.9%–48.2% of patients were asymptomatic. KDCA data from February to April 2020 showed that 38.6% of patients under the age of 20 were asymptomatic. Foreign studies reported that 66.4% of patients in an American study and 13% of patients in one meta-analysis were asymptomatic [4,10-12,15]. In our study, asymptomatic patients were similar to the finding in two of three studies on hospitalized Korean patients but lower than that reported in other studies. The lower number of asymptomatic patients in these three studies might stem from enrolling only patients who visited the hospital. Another Korean study with hospitalized children reported that 48.2% of patients were asymptomatic. Because the study was conducted on patients when all patients were transferred to community treatment centers or hospitals according to the guidelines of the Korean quarantine authorities, the rate may have been higher than other Korean studies with patients who visited hospital. Therefore, the real number of asymptomatic patients is expected to be higher than reported in this study.

There is a lack of consensus on the definition of long-lasting symptoms after acute COVID-19, and the prevalence varies widely [16]. Even when only studies investigating symptoms lasting more than 4 weeks are considered, the results differ between studies. A national cohort study of patients under 18 years of age in Denmark reported that 12%–51% of patients showed post-acute COVID-19 symptoms depending on age [17], and a prospective cohort study of patients aged 5–17 years in the United Kingdom found that 3%–5% experienced post-acute COVID-19 symptoms [13]. In the current study, 13.2% of all patients had post-acute COVID-19 symptoms, and this finding is similar to that of the Danish study. In a meta-analysis of several case-control studies that surveyed persistent symptoms after SARS-CoV-2 infection, symptoms, such as cough, abdominal pain, myalgia, diarrhea, fatigue, and dizziness, did not show statistically significant differences between the patient and control groups. Loss of smell, headache, sore throat, and sore eyes occurred more frequently in the patient group than in the control group. The authors argued that the incidence of persistent symptoms following SARS-CoV-2 infection may be much less than that reported in the literature [18]. The most frequent symptoms of post-acute COVID-19 in our study were cough and fatigue. Some of the cases among the 13.2% of post-acute COVID-19 cases observed in our study may not have been caused by SARS-CoV-2 infection because these variables did not differ between the patient and control groups in a previously mentioned meta-analysis. When analyzing the data of the participants in our study for the significant variables mentioned above, only five patients had post-acute COVID-19, and the frequency decreased to 1.6%. Therefore, the frequency of post-acute COVID-19 cases is expected to significantly reduce in future studies addressing this issue.

The disease course differs significantly between children and adults. It is speculated that this is due to age-related differences in the immune system, the level of expression of the angiotensin-converting enzyme 2 receptor, and the characteristics of the respiratory system [19]. An American study reported results similar to those of our study. Cough, rhinorrhea, dyspnea, myalgia, headache, sore throat, nausea or vomiting, abdominal pain, diarrhea, and loss of smell or taste were more frequently observed in those aged 10 years and older. Only fever was seen more frequently in children younger than 10 years of age [20]. In our study, the frequency of 12 out of 19 symptoms tended to increase with age, and no age-related trend was observed for six symptoms. Only fever tended to decrease with age, as observed in a previous study in the United States. We believe that this phenomenon reflects not only the hypothesis mentioned above but also the fact that symptoms can be expressed better as age increases.

Asthma was initially hypothesized to be a risk factor for severe COVID-19, given the association between asthma exacerbations and common respiratory viral diseases. Fortunately, however, the overall clinical outcomes of COVID-19 patients with asthma are similar to those of patients without asthma [21]. In a case-control study that compared asthma and non-asthma groups in COVID-19 patients aged 6–18 years, there was no statistically significant difference between the two groups in the incidence of cough and dyspnea during the acute period. The incidence of fever, sore throat, chest pain, and gastrointestinal problems were also similar to our results [22]. Unlike the acute phase symptoms, we observed that post-acute COVID-19 occurred more often in the asthma group than in the non-asthma group. One study of 29 children with a mean

age of 13 years showed that the prevalence of asthma was higher in COVID-19 patients who complained of respiratory symptoms for more than 6 weeks than in the general population under 18 years old [23]. In a prospective cohort study of approximately 1,000 adults with COVID-19 in the United States, asthma patients had a 1.54 times higher risk of developing post-acute COVID-19 [24]. This suggests that asthma may affect the development of prolonged symptoms after COVID-19. There is another opinion as well. In a retrospective cohort study with adult patients with COVID-19, 75% of those with asthma and 76.8% of those without asthma continue to complain of symptoms even 90 days after infection, and some researchers have asserted that post-acute COVID-19 does not occur more often in patients with asthma in their review article [21,25].

Even before the COVID-19 pandemic, cough, which was the most common symptom of post-acute COVID-19 in this study, was usually referred to as postinfectious cough if it persisted for more than 3 weeks following viral infection [26]. There are no studies comparing persistent symptoms including cough after viral infection in patients with and without typical asthma. However, there have been studies that analyzed patients who coughed over 3 weeks by dividing them into postinfectious cough and cough variant asthma. One study of 195 patients with prolonged cough in Japan reported that 99 patients (50.8%) were diagnosed with postinfectious cough, and 40 patients (20.5%) were diagnosed with cough variant asthma. Chinese research investigating 104 patients with subacute cough following cold reported that 45 patients (43.2%) were diagnosed with postinfectious cough, and 17 patients (16.3%) were diagnosed with cough variant asthma [27,28]. In both studies, the number of patients with cough variant asthma were smaller than that of postinfectious cough. It suggests that SARS-CoV-2 may have different effects in asthma unlike other respiratory viruses. However, since the previous two studies excluded patients already diagnosed with asthma, it is difficult to simply compare their results with that of our study. In the future, additional well-designed studies are needed to determine whether post-acute COVID-19, especially prolonged cough, is more prevalent in asthma patients than other viral infections.

One study suggested that the reason why post-acute COVID-19 is more observed in asthma is related to immunoglobulin. A prospective cohort study in Switzerland reported that asthma was associated with risk of developing post-acute COVID-19 (OR, 9.74; p=0.003), and IgG3 in asthma patients was significantly lower (p=0.038) than patients without asthma [29]. Authors of the study suggested that IgG3 secreted from B cells contributes to the development of post-acute COVID-19. This is also supported by an Italian cohort study that showed differences in epigenetic and transcriptional signatures in B cells between patients who did and did not develop post-acute COVID-19 [30].

Despite reports that the overall effectiveness of SARS-CoV-2 vaccination in children is 90%–100% and that it is more effective and safer in children than in adults [29,30], breakthrough infections may occur. In our study, 42 of the 73 patients eligible for vaccination (58%) were vaccinated, and 41 of them were infected with SARS-CoV-2 despite being fully vaccinated more than twice. One review article reported that breakthrough infections were milder than infections in the unvaccinated group [31]. Likewise, in our study, vaccinated adolescents had lower incidences of fever, vomiting, and fatigue than those of unvaccinated adolescents. Similar results were obtained after adjusting for age and sex, which are consistent with the results of previous studies. According to the UK Health Security Agency, of eight studies with COVID-19 patients, six showed that vaccinated patients less developed post-acute COVID than unvaccinated patients [32]. Our study did not show a significant difference between the two groups, contrary to previous studies. The results in this study cannot confirm the effectiveness of vaccination in adolescents and cannot refute or support earlier studies showing that vaccination may reduce post-acute COVID-19. Because our study included a small number of patients in the vaccinated and unvaccinated groups (38 and 31, respectively). Therefore, future studies should assess the effectiveness of vaccination, targeting only Korean children and adolescents. Such studies will hopefully counter and refute rumors and conspiracy theories spreading among the public.

This study had several limitations. First, the number of cases in this study was less than 1% of the 23,719 daily average number of cases of COVID-19 among Korean patients under the age of 20 reported in the first half of 2022; this sample size is too small to adequately represent Korean pediatric patients. Second, recall bias existed in our study because it was a retrospective study based on reports from medical records. Additionally, our data included missing

values, which was an obstacle to the statistical analysis. Finally, selection bias could not be excluded because only patients who visited a single tertiary healthcare center were included; thus, many patients with asymptomatic SARS-CoV-2 infection with no underlying diseases may not have been enrolled in this study. However, severely ill patients may have been underrecruited because our hospital was not COVID-19-dedicated.

Nevertheless, our report has the advantage of examining the duration of each symptom and frequency of post-acute COVID-19 in children and adolescents who visited a single center regardless of hospitalization. Additionally, we showed that the rate of post-acute COVID-19 was significantly higher in the asthma group than in the non-asthma group. In the case of vaccination, even if breakthrough infection occurred, they had milder symptoms compared to those who were not vaccinated. Our findings provide information on the clinical manifestations of COVID-19 in Korean children for patients and their caregivers. Our results also highlight the need to observe patients with asthma for more than 4 weeks. In the future, large-scale, long-term studies are required to more accurately identify the clinical features and prognosis of COVID-19 in Korean pediatric patients to reduce public anxiety and unnecessary socioeconomic costs.

Article information

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

Funding

None.

Author contributions

Conceptualization: JEJ, HLC, YYJ. Data curation: JEJ, YHK, NL, YK. Formal analysis: YYJ. Investigation: JEJ, YYJ. Methodology: Project administration; Resources; Software; Supervision: YYJ. Validation; Visualization: JEJ, YYJ. Writing - original draft: JEJ, YYJ. Writing - review & editing: YYJ. Approval of final manuscript: all authors.

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